Activation of patient-specific endogenous myocardial repair through the exosomes generated from the hypoxic iPSC-derived cardiomyocytes (iCMs).

Grant Award Details

Activation of patient-specific endogenous myocardial repair through the exosomes generated from the hypoxic iPSC-derived cardiomyocytes (iCMs).

Grant Type: Inception - Discovery Stage Research Projects

Grant Number: DISC1-08650

Project Objective: To leverage the novel methods, established workflow, and compelling preliminary data in our laboratory to test the central hypothesis that the exosomes salvage the injured myocardium in the peri-infarct region (PIR). The findings of the study would present a transformative approach to translate cell-free therapeutic strategy of iPSC-derivatives and may explain the restorative mechanism of the iCMs.

Investigator:

Name:	Phillip Yang
Institution:	Stanford University
Type:	PI

Disease Focus: Heart Disease

Human Stem Cell Use: iPS Cell

Cell Line Generation: iPS Cell

Award Value: $234,619

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Grant Application Details

Application Title: Activation of patient-specific endogenous myocardial repair through the exosomes generated from the hypoxic iPSC-derived cardiomyocytes (iCMs).

Public Abstract:

Research Objective

This proposal will provide direct evidence of clinical implementation of patient-specific iPSC products by validating the efficacy of autologous, cell-free exosome therapy.

Impact

Five-year survival of heart failure is a dismal 50% and is top diagnosis of hospital admission. Exosomes offer a feasible and effective cell-free therapy by activating endogenous myocardial repair.

Major Proposed Activities

- The exosomes from the injury and non-injury models of human iCMs are generated, quantified, isolated, and analyzed for their miRNA content.
- Functional benefit of injured and non-inured exosomes and their corresponding miRNAs is assessed following direct injection into the injured murine myocardium, using advanced MRI and molecular assays.
- Autologous exosomes and their miRNAs derived from the injured iCMs are re-administered to the iCMs to assess the efficacy of activating endogenous self-repair and elucidate the mechanism of action.
- Changes in the molecular, cellular and functional property of the injured iCMs are measured after the re-administration of the exosomes and miRNAs to determine the in vitro restorative effects.
- Changes in fibrosis, hypertrophy, remodeling, and apoptosis genes are measured by microarray, cell injury through flow cytometry, and contractile force via atomic force microscopy.
- Electrical activity is measured via patch clamp to quantitate the direct electrophysiologic effects of the exosomes on iCMs. The functional assays listed here are well established in our laboratory.

Statement of Benefit to California:

Five-year survival of heart failure (HF) is a dismal 50% and a leading diagnosis of hospital admission in California. Autologous exosomes may offer a feasible, effective therapy by activating endogenous repair of the injured heart. This study allows systematic analysis of the feasibility of cell-free therapeutic paradigm generated from patient- and injury-specific iPSC-derivatives. The exosomes will circumvent the challenges of stem cell therapy and provide effective therapy for all patients.
